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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	

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12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/782,588	KAIN ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-12,18-25 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-12,18-25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to papers filed 13 November 2002 in Paper No. 11 in which claims 1-4, 6-7, 9-12, 18-20 and 23-25 were amended and claim 26 was added. New claim 26 has been renumbered as claim 27 according to 37 C.F.R. 1.126. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 9 dated 13 June 2002 withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

Claims 1-4, 6-12, 18-25 and 27 are under prosecution.

Priority

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, Provisional Application 60/181,631 filed 2 February 2000 upon which priority is claimed does not provide adequate support under 35 U.S.C. 112 for claims 1-4, 6-12 and 18-25 of this application. Specifically, the '631 application does not teach or describe random distribution of microspheres on a substrate surface; does not teach or describe a distance between centers of a first and second microsphere of a subpopulation; and does not teach or describe a ratio of first and second subpopulations. Because the '631 application does not teach or describe the above limitations recited in the instant claims, the '631 application does not provide adequate support under 35 U.S.C. 112, for the instant claims. Therefore, the

effective filing date for the instant claims is the filing date of the instant application i.e. 12 February 2001.

Response to Applicant's Comments

3. Applicant argues that page 2, ¶ 5 the'631 application discloses a first and second subpopulation. The examiner has reviewed page 2 and acknowledges the disclosure of first and second subpopulations.

Applicant argues that support for the limitation "random distribution of microspheres on a substrate surface is provided on page 1, number 4, second and third paragraphs of the '631 application. The cited passage recites "randomly assembled Bead Arrays™ and Array of Arrays™". Applicant asserts that "randomly assembled array, in the context of this application, necessarily means that the microspheres are randomly distributed on the surface of the substrate because the arrays are bead based and assembly requires distribution of the beads on the surface of the substrate." The argument has been considered but is not found persuasive because in the recitation "randomly assembled arrays", randomly describes the assembly of the arrays. The recitation does not limit or require that the beads of the arrays to random distribution on a surface as instantly claimed. In contrast, the recitation "randomly assembled arrays encompasses any component of array assembly e.g. probe synthesis, probe attachment, substrate surface modification and/or microfabrication. As such, the cited passage does not provide support for the instantly claimed random distribution of microspheres on a substrate surface.

Applicant states that the '631 (at the bottom of page 1) provides support to the instantly claimed distance between centers of first and second microspheres of at least 5μ m. The cited passage describes bead spacing of from <15μ m to 15-20μ m. The cited passage does not teach or describe a distance between centers as instantly claimed. The instantly claimed distance between centers describes a measurement between the center of one bead to the center of another bead. This measurement encompasses bead size and distance between the

beads and further encompasses a measurement wherein no spacing is present between beads. In contrast, the cited passage merely teaches a spacing between the beads. As such, the '631 application does not provide support of the instant claims.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-4, 6-7, 9-12, 18-20 and 23-25are rejected under 35 U.S.C. 102(b) as being anticipated by Brenner (U.S. Patent No. 5,863,722, issued 26 January 1999).

Regarding Claim 1, Brenner discloses a composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μm (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 50μ m (Column 10, lines 30-35 and Column 20, lines 32-35); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a

second bioactive agent wherein said microspheres are randomly distributed on said surface (Column 20, lines 42-46) wherein the substrate comprise the dimensions of a microscope slide (Column 19, lines 55-60 and Fig. 5).

Regarding Claim 2, Brenner discloses the composition wherein the sites are separated by a distance of less than 25 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 25μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 3, Brenner discloses the composition wherein the sites are separated by a distance of less than 15 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 15μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 4, Brenner discloses the composition wherein the sites are separated by a distance of at least about 5 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is at least about 5μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 6, Brenner discloses the composition wherein the distance between centers of a first and second subpopulations is at least 5 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is at least about 5μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 7, Brenner discloses the composition wherein the distance between a first and second microspheres is less than 100μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 100μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 9, Brenner discloses the composition wherein the distance between a first and second microspheres is less than 100μ m (i.e. separated by a space equal to

microsphere diameter wherein the diameter of the microsphere is less than 100μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 10, Brenner discloses the composition wherein the distance between a first and second microspheres is less than 50μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 50μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 11, Brenner discloses the composition wherein the distance between a first and second microspheres is less than 15μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 15μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 12, Brenner discloses the composition wherein the sites are separated by a distance of at least about 5 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is at least about 5μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 18, Brenner discloses a method for making a composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μm (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 50μ m (Column 10, lines 30-35 and Column 20, lines 32-35); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface (Column 20, lines 42-46) wherein the substrate comprise the dimensions of a microscope slide (Column 19, lines 55-60 and Fig. 5).

Regarding Claim 19, Brenner discloses the method wherein the sites are separated by a distance of less than 25 μ m (i.e. separated by a space equal to microsphere diameter wherein

the diameter of the microsphere is less than 25μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 20, Brenner discloses the method wherein the sites are separated by a distance of less than 15 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 15μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 23, Brenner discloses the composition wherein the distance between centers of a first and second subpopulations is at least 5 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is at least about 5μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 24, Brenner discloses the composition wherein the distance between centers of a first and second subpopulations is at least 15 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is at least about 15μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

Regarding Claim 25, Brenner discloses the method wherein the distance between a first and second microsphere is at least 50 μ m (i.e. separated by a space equal to microsphere diameter wherein the diameter of the microsphere is less than 50μ m (Column 10, lines 30-35 and Column 20, lines 32-35).

6. Claims 1-3, 6-11, 18-20, 23 and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by Fan et al (U.S. Patent Application Publication No. 2002/0132241 A1, filed 7 February 2000).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Regarding Claim 1, Fan et al disclose a composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μ (¶ 189-190); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface (¶ 196 and 216) wherein the substrate comprise the dimensions of a microscope slide (¶ 62, lines 5-8).

Regarding Claim 2, Fan et al disclose the composition wherein the sites are separated by a distance of less than 25 μ m (¶ 189-190).

Regarding Claim 3, Fan et al disclose the composition wherein the sites are separated by a distance of less than 15 μ m (¶ 189-190).

Regarding Claim 6, Fan et al disclose the composition wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 5 μ m (¶ 189-190).

Regarding Claim 7, Fan et al disclose the composition wherein the distance between a first and second microspheres is less than 100μ m (¶ 189-190).

Regarding Claim 8, Fan et al disclose the composition wherein the substrate further comprises first and second assay locations (i.e. wells) and wherein said first and second subpopulations are distributed in said assay locations (¶ 192-198).

Regarding Claim 9, Fan et al disclose the composition wherein the distance between a first and second microsphere is less than 100μ m (¶ 189-190).

Regarding Claim 10, Fan et al disclose the composition wherein the distance between a first and second microsphere is less than 50μ m (¶ 189-190).

Regarding Claim 11, Fan et al disclose the composition wherein the distance between a first and second microsphere is less than 15μ m (¶ 189-190).

Regarding Claim 18, Fan et al disclose a method for making a composition comprising: providing a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μm (¶ 189-190); and randomly distributing a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive (¶ 196 & 216) wherein the substrate comprise the dimensions of a microscope slide (¶ 62, lines 5-8).

Regarding Claim 19, Fan et al disclose the method wherein said wells are separated by distance of less than 25μ m (¶ 189-190).

Regarding Claim 20, Fan et al disclose the method wherein said wells are separated by distance of less than 15μ m (¶ 189-190).

Regarding Claim 23, Fan et al disclose the composition wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 5 μ m (¶ 190).

Regarding Claim 27, Fan et al disclose the method wherein the discrete sites are wells (¶ 194).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 4, 12, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fan et al (U.S. Patent Application Publication No. 2002/0132241 A1, filed 7 February 2000) in view of Brenner (U.S. Patent No. 5,863,722, issued 26 January 1999).

Regarding Claims 4 and 12, Fan et al teach the composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μ (¶ 189-190); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface (¶ 196 and 216) wherein the substrate comprise the dimensions of a microscope slide (¶ 62, lines 5-8) said sites are separated by a distance of less than 15μ m i.e. center-to-center of 5μ m (¶ 190) but they are silent regarding a separation of at least 5μ m. However, microsphere spacing on the surface of a substrate being at least 5μ m was well known in the art at the time the claimed invention was made as taught by Brenner who teach the preferred microspheres have a diameter of 1-1000μ m (Column 10, lines 30-35) are separated by a space equal to their diameter to facilitate resolution of individual microspheres (Column 20, lines 27-46). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the spacing suggested by Brenner

and to space the microsphere by at least 5μ m for the expected benefit of permitting individual resolution of the microspheres as taught by Brenner (Column 20, lines 27-46).

Regarding Claims 24 and 25, Fan et al teach a method for making a composition comprising: providing a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μm (¶ 189-190); and randomly distributing a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive (¶ 196 & 216) wherein the substrate comprise the dimensions of a microscope slide (¶ 62, lines 5-8) said sites are separated by a distance of less than 15μ m i.e. center-to-center of 5μ m (¶ 190) but they are silent regarding a separation of at least 5μ m. However, microsphere spacing on the surface of a substrate being at least 5μ m was well known in the art at the time the claimed invention was made as taught by Brenner who teach the preferred microspheres have a diameter of 1-1000μ m (Column 10, lines 30-35) are separated by a space equal to their diameter to facilitate resolution of individual microspheres (Column 20, lines 27-46). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the spacing suggested by Brenner and to space the microsphere by at least 5μ m for the expected benefit of permitting individual resolution of the microspheres as taught by Brenner (Column 20, lines 27-46).

9. Claims 1-4, 6-12, 18-20 and 23-25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 98/40726, published 17 September 1998) in view of Noonan

et al (U.S. Patent No. 6,129,896, filed 17 December 1998) and Van Ness et al (U.S. Patent No. 6,248,521, issued 19 June 2001).

Regarding Claim 1, Walt et al teach a composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μ (Fig. 5); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface (page 17, line 13-page 18, line 24). Walt et al teach that the substrate comprises a plurality of fibers arranged into a bundle for optimal observation via their microscope objective lens (page 19, lines 15-25) but they do not teach their substrate comprises the dimensions of a microscope slide. However, it was well known in the art at the time the claimed invention was made that fiber optic bundles can be formatted to desired dimensions as taught by Noonan et al. (Abstract) and Van Ness et al teach a motivation for formatting the substrate to have the dimensions of a microscope slide i.e. a substrate having the dimensions of a glass slide is easily illuminated and detected using a microscope (Column 10, lines 27-41). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the glass slide dimensioned substrate of Van Ness et al to the substrate of Walt et al and to format the substrate comprising microspheres to the format of a glass slide for the obvious benefits of facility of illumination and detection using a microscope as taught by Van Ness et al (Column 10, lines 27-41).

The courts have stated that claimed dimensions of a known device do not distinguish over the prior art device when the claimed device would not perform differently from the prior art device. *In Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

The courts have stated that absent evidence to the contrary, a particular configuration of a known device is a matter of choice which would have been obvious to one skilled in the art. *In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966) (The court held that the configuration of the claimed disposable plastic nursing container was a matter of choice which a person of ordinary skill in the art would have found obvious absent persuasive evidence that the particular configuration of the claimed container was significant.).

Regarding Claim 2, Walt et al teach the composition wherein the sites are separated by a distance of less than 25 μ m (Fig. 5).

Regarding Claim 3, Walt et al teach the composition wherein the sites are separated by a distance of less than 15 μ m (Fig. 5).

Regarding Claim 4, Walt et al teach the composition wherein said sites are separated by a distance of less than 15μ m (Fig. 5) but they do not teach the separation is at least 5μ m. However, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation distance of Walt et al using routine experimentation to thereby derive an optimal separation distance (e.g. at least 5m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 6, Walt et al teach the composition wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 5 μ m (Fig. 5).

Regarding Claim 7, Walt et al teach the composition wherein the distance between a first and second microspheres is less than 100μ m (Fig.5).

Regarding Claim 8, Walt et al teach the composition wherein the substrate further comprises first and second assay locations (i.e. wells) and wherein said first and second subpopulations are distributed in said assay locations (page 22, lines 8-30).

Regarding Claim 9, Walt et al teach the composition wherein the distance between a first and second microsphere is less than 100μ m (Fig. 5).

Regarding Claim 10, Walt et al teach the composition wherein the distance between a first and second microsphere is less than 50μ m (Fig. 5).

Regarding Claim 11, Walt et al teach the composition wherein the distance between a first and second microsphere is less than 15μ m (Fig. 5).

Regarding Claim 12, Walt et al teach the composition wherein the distance between centers of a first and second subpopulations is at least 2.2m m (Fig. 5) but they do not specifically teach the distance between the microspheres is at least 5μ m. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Walt et al using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5μ m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

Regarding Claim 18, Walt et al teach a method for making a composition comprising: providing a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μm (Fig. 5); and randomly distributing a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive (page 17, line 13-page 18, line 24). Walt et al teach that the substrate comprises a plurality of fibers arranged into a bundle for optimal observation via their microscope objective lens (page 19, lines 15-25) but they do not teach their substrate comprises the dimensions of a microscope slide. However, it was well known in the art at the time the claimed invention was made that fiber optic bundles can be formatted to desired dimensions as taught by Noonan et al. (Abstract) and Van Ness et al teach a motivation for formatting the substrate to have the dimensions of a microscope slide i.e. a substrate having the dimensions of a glass slide is easily

illuminated and detected using a microscope (Column 19, lines 27-41). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the glass slide dimensioned substrate of Van Ness et al to the substrate of Walt et al and to format the substrate comprising microspheres to the format of a glass slide for the obvious benefits of facility of illumination and detection using a microscope as taught by Van Ness et al (Column 19, lines 27-30).

The courts have stated that claimed dimensions of a known device do not distinguish over the prior art device when the claimed device would not perform differently from the prior art device. *In Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

The courts have stated that absent evidence to the contrary, a particular configuration of a known device is a matter of choice which would have been obvious to one skilled in the art. *In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966) (The court held that the configuration of the claimed disposable plastic nursing container was a matter of choice which a person of ordinary skill in the art would have found obvious absent persuasive evidence that the particular configuration of the claimed container was significant.).

Regarding Claim 19, Walt et al teach the method wherein said wells are separated by distance of less than 25μ m (Fig. 5).

Regarding Claim 20, Walt et al teach the method wherein said wells are separated by distance of less than 15μ m (Fig. 5).

Regarding Claim 23, Walt et al teach the composition wherein the distance between centers (i.e. pitch) of a first and second subpopulations is at least 5 μ m (Fig. 5).

Regarding Claim 24, Walt et al teach the method wherein the distance between centers of a first and second subpopulations is at least 5μ m (Fig. 5) but they do not specifically teach the distance between centers is at least 15μ m. It would have been obvious to one of ordinary

skill in the art at the time the claimed invention was made to modify the distance between centers of the first and second subpopulations on the substrate of Walt et using routine experimentation to thereby derive an optimal center-to-center distance (e.g. at least 5m m and at least 15m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 25, Walt et al teach the method wherein the distance between microspheres is at least 5μ m (Fig. 5) but they do not specifically teach the distance between microspheres is at least 50m m. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the distance between microspheres on the substrate of Walt using routine experimentation to thereby derive an optimal distance (e.g. at least 50m m) for the obvious benefits of optimizing experimental conditions to thereby maximize experimental results.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 27, Walt et al teach the method wherein the discrete sites are wells (page 7, lines 5-9).

10. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 998/40726, published 17 September 1998) in view of Noonan et al (U.S. Patent No.

6,129,896, filed 17 December 1998) and Van Ness et al (U.S. Patent No. 6,248,521, issued 19 June 2001) as applied to Claim 18 above and further in view of Gentalen et al (U.S. Patent No. 6,306,643 B1, filed 24 August 1998).

Regarding Claims 21 and 22, Walt et al is silent regarding a ratio between microsphere subpopulations. However, ratios of subpopulations were well known in the art at the time the claimed invention was made as taught by Gentalen et al who teach that subpopulation ratios are derived based on experimental design (Column 11, lines 13-44 and Claim 9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the ratio of first and second subpopulations based on experimental design to thereby optimize experimental results. For example, for an experiment designed to detect nucleic acid sequences expressed in low copy number, the skilled practitioner in the art would have been motivated to provide subpopulations of nucleic acid microspheres in a ratio of 1:36 or 1:100 (high copy number sequence:low copy number sequence) to thereby detect the low copy number sequence without signal interference from the high copy number sequence. In this experimental design it would have been obvious to one of ordinary skill in the art to modify the low copy to high copy number ratio using routine experimentation to thereby optimize experimental conditions and to maximize detection of low copy number.

11. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner (U.S. Patent No. 5,863,722, issued 26 January 1999) in view of Gentalen et al (U.S. Patent No. 6,306,643 B1, filed 24 August 1998).

Regarding Claims 21 and 22, Brenner teaches the method for making a composition comprising a substrate with a surface comprising discrete sites said sites separated by a distance of less than 50μm (i.e. separated by a space equal to microsphere diameter wherein

the diameter of the microsphere is less than 50μ m (Column 10, lines 30-35 and Column 20, lines 32-35); and a population of microspheres comprising at least a first and second subpopulation wherein said first subpopulation comprises a first bioactive agent and said second subpopulation comprises a second bioactive agent wherein said microspheres are randomly distributed on said surface (Column 20, lines 42-46) wherein the substrate comprise the dimensions of a microscope slide (Column 19, lines 55-60 and Fig. 5). Brenner is silent regarding a ratio between microsphere subpopulations. However, ratios of subpopulations were well known in the art at the time the claimed invention was made as taught by Gentalen et al who teach that subpopulation ratios are derived based on experimental design (Column 11, lines 13-44 and Claim 9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the ratio of first and second subpopulations based on experimental design to thereby optimize experimental results. For example, for an experiment designed to detect nucleic acid sequences expressed in low copy number, the skilled practitioner in the art would have been motivated to provide subpopulations of nucleic acid microspheres in a ratio of 1:36 or 1:100 (high copy number sequence:low copy number sequence) to thereby detect the low copy number sequence without signal interference from the high copy number sequence. In this experimental design it would have been obvious to one of ordinary skill in the art to modify the low copy to high copy number ratio using routine experimentation to thereby optimize experimental conditions and to maximize detection of low copy number.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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Patent Examiner
Art Unit: 1634
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